UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

SANOFI-AVENTIS, SANOFI-SYNTHELABO INC., and BRISTOL-MYERS SQUIBB SANOFI PHARMACEUTICALS HOLDING PARTNERSHIP,	:	
Plaintiffs,	:	**02-CV-2255 (SHS)**
v.	:	
APOTEX INC. and APOTEX CORP.,	:	
Defendants.	:	**ELECTRONICALLY FILED**

AMICUS CURIAE BRIEF OF NATIONAL ASSOCIATION OF CHAIN DRUG STORES IN OPPOSITION TO PLAINTIFFS' MOTION FOR PRELIMINARY INJUNCTION

Amicus Curiae, National Association of Chain Drug Stores, submits this memorandum in opposition to Plaintiffs' motion for a preliminary injunction to halt the sale of an FDA-approved generic version of Plavix. Plaintiffs have already received the benefit of an automatic 30-month stay mandated by Congress and of an additional hiatus from competition, which they obtained in defiance of a Consent Order entered with the Federal Trade Commission. Generic competition for Plavix is overdue, and this Court should not halt it. The Court should deny Plaintiffs' motion for preliminary injunction because they come to the Court with unclean hands and because entry of an injunction would cause irreparable harm to retail pharmacies and consumers.[1]

[1] While there are additional reasons for denying Plaintiffs' motion for a preliminary injunction, those arguments will be addressed by Defendant Apotex. NACDS will not repeat

INTEREST OF AMICUS CURIAE

The National Association of Chain Drug Stores ("NACDS") represents the nation's leading retail chain pharmacies and suppliers, helping them better meet the changing needs of their patients and customers. NACDS members operate more than 32,000 pharmacies, employ 112,000 pharmacists, fill more than 2.1 billion prescriptions yearly, and have annual sales of over $500 billion. Other members include more than 1000 suppliers of products and services to the chain drug industry. For more information about NACDS, visit www.nacds.org.

Plavix (clopidogrel bisulfate) is one the most-frequently dispensed pharmaceutical products in retail pharmacies. In 2005, Plavix ranked seventh on the list of retail pharmacy's top selling prescription pharmaceuticals. *See Top 200 Brand-Name Drugs by Retail Dollars in 2005*, Drug Topics, Mar. 6, 2006.

Apotex's launch of generic clopidogrel bisulfate has allowed NACDS members to offer a less expensive, generic alternative to consumers. As of last week, those consumers have been able to purchase this generic product at a savings of upwards of 25% to 30% off the price they had paid for branded Plavix. Plaintiffs are asking this Court to eliminate that cost-saving opportunity. In doing so, Plaintiffs focus on the effect this launch will have on *them* if the '265 patent is found to be valid. But Plaintiffs have already unlawfully helped themselves to more pre-trial exclusion of competition than they are entitled to. And there would be more weighty effects on retail pharmacies and consumers if the Court grants the requested injunction and the patent is later found to be invalid. This brief gives voice to these latter consequences and to the strong public interest in preserving the opportunity to purchase generic clopidogrel bisulfate.

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those arguments herein.

BACKGROUND

A. Consumers Benefit From Generic Competition.

Generic drugs save consumers upwards of $8 to $10 billion dollars each year. Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry* (July 1998) ("CBO Study"). As numerous academic and government studies have documented, generic drugs typically enter the market at a much lower price than their brand name counterparts and quickly replace brand name sales. A 1998 study by the Congressional Budget Office, for example, compared prices for brands and generics for twenty-one brand drugs that faced generic competition between 1991 and 1993. *Id.* The CBO Study found that the average generic prescription price was *less than half* the average brand price. *Id.* at 28-31.

A more recent study found that the average price difference had increased:

> In 1993 the average cost for a brand name prescription drug was 275% higher than the average generic ($35.28 versus $12.82). By 2000 this difference had grown to nearly 340% ($65.29 versus $19.33).

See Kirking et al., *Economics and Structure of the Generic Pharmaceutical Industry*, 41 J. Amer. Pharm. Assoc. 578, 579 (2001).

The price competition engendered by generic drug manufacturers benefits all purchasers of the drug, at all levels of the distribution chain, who are able to buy the same chemical substance at much lower prices. Retail pharmacies, such as those owned and operated by NACDS members, substitute generic drugs for brand-name drugs whenever appropriate in order to lower their own costs and those of their customers. When generic Zithromax entered the market, for example, retail pharmacies switched more than 90% of the product to the generic within

four months after generic entry. *Hopes High as 72 Drugs Are Set to Lose Patents*, 28:4 Chain Drug Rev. 69 (Feb. 27, 2006) (attached as Exhibit A).

B. Generic Clopidogrel Bisulfate.

The launch of Apotex's clopidogrel bisulfate product last week has allowed NACDS members to offer their customers a choice. Customers presenting a prescription for clopidogrel bisulfate can now choose whether to fill that prescription with the branded product, Plavix, or Apotex's generic product. To date, tens of thousands of those customers have chosen the generic product and have saved 25% to 30% by doing so. Current estimates are that the pharmacies of NACDS members are filling over 50% of the clopidogrel bisulfate prescriptions with the Apotex product, and that percentage keeps growing daily.

Generic competition for clopidogrel bisulfate is long overdue. More than four years have elapsed since Apotex first lodged its ANDA challenge to the validity of the '265 patent. As the Court is aware, the brand manufacturers lobbied for and received from Congress an automatic 30-month stay that prohibits the FDA from approving a generic product while patent litigation is pending. *See* 21 U.S.C. § 355(j)(5)(B)(iii). Final FDA approval for Apotex's product finally came seven months ago, in January 2006.

Unsatisfied with the 30-month stay granted by Congress and the further delay attendant on FDA's approval process, BMS/Sanofi bought an additional hiatus from competition. BMS/Sanofi entered into an Agreement with Apotex, agreeing to make multi-million dollar payments to Apotex in exchange for Apotex's agreement to not market its generic product.[2] As

[2] That agreement is currently the subject of multiple lawsuits, and members of NACDS are among parties that have brought those antitrust challenges. *See CVS Pharmacy, Inc. v. Sanofi-Aventis*, No. 1:06-cv-427 (S.D. Ohio); *Kroger Co v. Sanofi-Aventis*, No. 1:06-cv-163

discussed in detail below, BMS/Sanofi entered into this Agreement in defiance of a Consent Order entered with the Federal Trade Commission ("FTC") on April 14, 2003.

Last week, Apotex finally launched its product, after the July 31 deadline for federal and state regulatory approval of the Agreement passed. In an effort to stop that competition, BMS/Sanofi is now seeking to enlist this Court's aid.

ARGUMENT

A. A Preliminary Injunction is Inappropriate in Light of Plaintiffs' Unclean Hands.

A preliminary injunction is an equitable remedy, and thus is subject to the maxim: He who comes into equity must come with clean hands. *See TCPIP Holding Co., Inc. v. Haar Comm's, Inc.,* 244 F.3d 88, 102-03 (2d Cir. 2001) (preliminary injunction may be denied when party has unclean hands); *Estate of Lennon by Lennon v. Screen Creations, Ltd.*, 939 F. Supp. 287, 293 (S.D.N.Y. 1996) (denying preliminary injunction in spite of "compelling arguments that [plaintiffs] have a likelihood of success on the merits and will be irreparably harmed without preliminary relief" because of plaintiffs' unclean hands).

Plaintiffs come to this Court with unclean hands. Plaintiffs could have filed this preliminary injunction request seven months ago, when Apotex was granted final FDA approval. Instead, Plaintiffs chose to pay Apotex, their potential competitor, to stay off the market. This pay-off agreement was in direct contravention of a Consent Order that BMS entered into with the FTC in connection with a previous pay-off agreement.[3] BMS entered into the Consent Order to

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(S.D. Ohio); *In re Plavix Direct Purchaser Antitrust Litig.*, No. 1:06-cv-202 (S.D. Ohio). Those challenges are pending in the Southern District of Ohio.

[3] The weight of authority holds that such pay-off agreements violate Section 1 of the Sherman Act. Three courts, a unanimous FTC, the nation's leading antitrust scholars, and a bipartisan Congress have concluded that such agreements are either *per se* or presumptively

resolve claims that, *inter alia*, BMS had violated the Sherman Act by paying a competitor not to enter the market with a generic version of BMS's drug, BuSpar. *See In the Matter of Bristol-Myers Squibb Co.*, No. C-4076, Consent Order (Apr. 14, 2003 F.T.C.) (attached as Exhibit B). That Consent Order provides that BMS is enjoined "from being a party to any Agreement in which . . . [t]he NDA Holder provides anything of value to the alleged infringer; and . . . [t]he ANDA Filer agrees to refrain during part or all of the course of the litigation from selling the ANDA Product, or any Drug Product containing the same active chemical ingredient as the ANDA Product." *Id.* at 11.

That is exactly what BMS agreed to do here. In an Agreement dated March 17, 2006, BMS agreed to make multi-million dollar payments to Apotex in exchange for Apotex's agreement to stay off the market for a period of time. The Agreement provides that Apotex will suspend any efforts to bring generic clopidogrel bisulfate to market at least until after the FTC and State Attorneys General completed their regulatory review of the Agreement. Agreement,

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anticompetitive. *See In re Cardizem CD Antitrust Litig.*, 332 F.3d 896 (6th Cir. 2003); *Andrx Pharmaceuticals, Inc. v. Biovail Corp. Int'l*, 256 F.3d 799 (D.C. Cir. 2001); *In re K-Dur Antitrust Litigation*, 338 F.Supp.2d 517 (D.N.J.2004); I Hovenkamp, et al., IP and Antitrust 7.4e2 (2005); Carl Shapiro, *Antitrust Analysis of Patent Settlements Between Rivals,* 17 Antitrust 70 (2003); David A. Balto, *Pharmaceutical Patent Settlements: The Antitrust Risks*, 55 Food and Drug L.J. 321 (2000); Remarks of Sen. Hatch, Cong. Rec. of July 20, 2002 at S7566 ("As coauthor of the [Hatch-Waxman Act], I can tell you that I find these type of reverse payment collusive arrangements appalling."); Remarks of Sen. Hatch, Cong. Rec. of July 20, 2002 at S7566 (commending the FTC "for creating a climate unfriendly to the execution of any additional collusive deals not to compete between generic and brand name companies"). One court has concluded that such agreements are not presumptively unlawful. *Schering-Plough Corp. v. Federal Trade Comm'n*, 402 F.3d 1056 (11th Cir. 2005). The status of such agreements in this Circuit is currently being litigated. *See In re Tamoxifen Citrate Antitrust Litig.*, 429 F.3d 370 (2d Cir. 2005), *petition for reh'g en banc pending*, No. 03-7641; *see also In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 363 F. Supp. 2d 514 (E.D.N.Y. 2005), *appeal and petition for hearing en banc docketed*, No. 05-2851 (2d Cir.). Regardless of whether the BMS/Sanofi agreement with Apotex violated the Sherman Act -- an issue that this Court need not decide -- it violated the clear terms of the FTC Consent Order.

¶ 19 ("Apotex agrees that it will not launch a generic clopidogrel product during the time of the Regulatory Review") (attached as Exhibit C).[4] In exchange, Sanofi, on behalf of itself and BMS,[5] agreed to make substantial payments to Apotex. The payment amounts varied depending upon whether the regulators cleared the Agreement. If the regulators did not clear the Agreement, those payments would total at least $60 million. *Id.* at ¶ 18. If the regulators did clear the Agreement, the payments would total up to $40 million. *Id.* at ¶ 13. This is the very type of agreement to "refrain during part or all of the course of the litigation from selling the ANDA Product" that the FTC Consent Order prohibits. *See* Consent Order at 11, Exhibit B.

On May 26, 2006, the parties entered into a Modified Agreement, but even that Modified Agreement violates the Consent Order. While the $60 million payment term was eliminated, the Modified Agreement still provides that "Apotex agrees that it will not launch a generic clopidogrel product during the time of the Regulatory Review." Modified Agreement, ¶ 15 (attached as Exhibit D). The Modified Agreement also provides that Sanofi will pay Apotex up to $500,000 if the regulators do not clear the Agreement. *Id.* at ¶ 14. Moreover, by the time the parties entered into the Modified Agreement, significant damage to consumers had already been done. The trial in this matter had been scheduled to begin in April 2006. The *original* Agreement had the effect of moving that trial off the Court's calendar, and the trial still has not been re-scheduled.

BMS/Sanofi could have negotiated a proposed agreement sufficiently in advance

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[4] Certain of the Agreement's terms become effective only after the FTC and State Attorneys General complete their regulatory review and indicate that they have cleared the Agreement. Agreement, ¶ 17, Exhibit C. The requirements that Apotex remain off the market and that BMS/Sanofi pay Apotex if regulatory approval of the agreement is denied were not among those provisions.

[5] *See* Agreement at p. 7, Exhibit C.

of Apotex receiving final FDA approval so as to permit FTC regulatory review to be completed *before* Apotex got final FDA approval. Or BMS/Sanofi could have sought this preliminary injunction in January 2006, upon Apotex's gaining final FDA approval. Or BMS/Sanofi could have negotiated an agreement with Apotex that did not include a payment to Apotex to refrain from marketing its product pending regulatory review of the Agreement. BMS/Sanofi did not do any of these things. Instead, they negotiated an Agreement that required Apotex to stay off the market in exchange for monetary payment. That Agreement thereby bought BMS/Sanofi months of hiatus from competition to which they were not entitled, in direct contravention of the Consent Order.

BMS/Sanofi obtained through unlawful self-help the very pre-trial exclusion of competition that they now ask this Court to grant. They come to the Court with unclean hands and are not entitled any equitable relief. *See Tempo Music, Inc. v. Myers,* 407 F.2d 503, 507 (4th Cir.1969) (violation of consent order constitutes unclean hands); *United States v. Int'l Bhd. of Teamsters*, 816 F.Supp. 864, 871 (S.D.N.Y. 1992) (violation of settlement agreement constitutes unclean hands); *Sony Corp. v. S.W.I. Trading, Inc.* 104 F.R.D. 535, 541 (S.D.N.Y. 1985) (same).

B. Granting the Requested Injunction Would Harm Retail Pharmacies and Consumers.

Even if Plaintiffs' unclean hands could be somehow ignored, ample reason exists to deny the requested preliminary injunction. Granting the requested injunction would force consumers and retail pharmacies to once again fill their clopidogrel bisulfate requirements with higher-priced, branded Plavix. The resulting harm includes economic loss that is not compensable in money damages. The harm also includes a litany of other intangibles losses. Each of these harms counsels against the entry of such injunction.

1. For at least a portion of the people who are prescribed clopidogrel bisulfate, removing the availability of the generic may prevent them from filling their prescriptions altogether, or at least cause them to take less of the medicine than they should. This obviously imposes an enormous human loss, for which the patients cannot receive adequate after-the-fact compensation.

There is a well-documented "deadweight loss" phenomenon in the pharmaceutical marketplace whereby the high price of prescriptions causes consumers to either decline to purchase the product or to purchase less than they should and split tablets or skip doses. *See, e.g.*, Schur, et al., *Lack of Prescription Coverage Among the Under 65: A Symptom of Underinsurance,* Issue Brief, Commonwealth Fund Task Force on the Future of Health Insurance, 2004, p.3 (attached as Exhibit E); *Prescription Drugs: A Vital Component of Healthcare*, Data Profile v. 5 (Georgetown University Center on Aging and Society, 2002) p. 4 (attached as Exhibit F). These losses are borne principally by the elderly, the poor and the uninsured or underinsured.

For example, one study found that the high price of medicines caused 22% of adults to refuse to have a prescription filled. The percentage rose to 46% for those whose out-of-pocket costs were $151 or more per month. *Higher Out-Of-Pocket Costs Cause Massive Non-Compliance in the Use of Prescription Drugs, and This is Likely to Grow*, 2:22 Health Care News (Dec. 6, 2002) (attached as Exhibit G). Similarly, 46% of adults with high out-of-pocket costs use less of a prescribed medication because of cost. *Id.* The results are fully confirmed by a host of academic research, which also finds that mortality, self-reported pain, worsening medical condition, and other adverse health effects all result from patients' decisions "not [to] comply with physicians' medication recommendations because of high costs." T. Rice & K.

Matsuoka, *The Impact of Cost-Sharing On Appropriate Utilization and Health Status: A Review of the Literature On Seniors*, 61:4 Med. Care Research & Rev. 415, 427-28 (Dec. 2004) (attached as Exhibit H); *see also id.* at 441 ("our literature review strongly suggests that increased cost-sharing tends to reduce the appropriate use of prescription drugs"). These are the real-world costs of granting the requested preliminary injunction.

Plavix is exactly the type of expensive product that results in enormous deadweight loss. The current Average Wholesale Price of a bottle of 30 tablets is $146.05. And that price is on the rise. Eight years ago, the Average Wholesale Price for a bottle of 30 tablets was $86.75, nearly 70% less than it is today. Because branded Plavix is so expensive, entry of the requested injunction will result in elimination of the only alternative for many consumers to obtain the necessary medication.

The human cost of that result will not be calculable. Moreover, these "deadweight losses" -- the losses resulting from the quantity not sold -- are generally not remediable even by the direct purchasers (wholesalers and retail pharmacies) under antitrust law. *See* ABA Section of Antitrust Law, PROVING ANTITRUST DAMAGES, at p. 198 (1996) ("there is no practical way to measure theoretically-accurate damages for the quantity not sold") (attached as Exhibit I); *see also Montreal Trading v. IMAX*, 661 F.2d 864, 867-68 (10th Cir. 1981). Thus, even if it is later established that BMS/Sanofi's conduct was so egregious as to violate the antitrust law, these enormous human and economic losses will likely go completely unremedied by either the direct purchasers or the ultimate consumers.

2. NACDS members and other direct purchasers may suffer uncompensable losses not only on quantities not sold but also on the quantities that *are* sold. Plaintiffs focus upon a world in which the '265 patent is eventually found by this Court to be valid. But the

entire purpose of this litigation is to determine *whether* the '265 patent is valid – an issue that Apotex has hotly contested for the past four years. If Plaintiffs are wrong and the '265 patent is later found to be invalid, removing Apotex's generic product from the market will have resulted in purchasers being overcharged for clopidogrel bisulfate. While the patent laws will have established that the '265 patent is invalid and thus that generic competition should not have been excluded, *those patent laws will not provide any avenue for harmed purchasers to recover the overcharges they paid.* The antitrust laws allow such a recovery under certain circumstances, but a court could find that BMS/Sanofi's conduct was not egregious enough to state an antitrust claim. *See, e.g., Nobelpharma AB v. Implant Innovations, Inc.*, 141 F.3d 1059, 1068 -69 (Fed. Cir. 1998) (antitrust claimant must show all the elements of a Section 2 claim, plus that the patentee obtained the patent by knowingly and willfully misrepresenting facts to the PTO, plus that the patent would not have issued but for the fraud). As such, purchasers may find themselves in a "gap" in the law: victims of an exclusion of competition that was wrongful under the patent law but that is not actionable under the antitrust law. We estimate that the unrecoverable harm in this circumstance would be more than $80 million for each month that the injunction is in place.[6]

3. Granting the injunction is likely to expose NACDS members to further harm in the form of the loss of customers' good will. Plavix is a medication that is refilled by patients month after month, over an extended period of time. Thousands of retail pharmacy customers have lowered the cost of their prescriptions by switching from branded Plavix to Apotex's clopidogrel bisulfate product. Stopping the sale of Apotex's clopidogrel bisulfate

[6] This calculation assumes an average generic penetration rate of 75%, a generic discount of 45% off the brand price, and a market of $3 billion per year (at the brand price).

product will mean that the next time those customers return to refill their prescriptions, they will have to pay more for the higher priced branded Plavix product. Since that money is being paid to the retail pharmacies, any frustration or anger those customers feel likely will be directed at those pharmacies. The good will that retail pharmacies have worked hard to build thus will be threatened by this injunction.

4. Customers also may be confused when they learn that the Apotex generic product is no longer available. Customers' familiarity with the withdrawal of products from the market may be limited to withdrawals due to safety reasons. No amount of explanation by pharmacists may be enough to convince customers that the product was not pulled due to safety reasons. This requested injunction thus may cause unnecessary customer confusion and anxiety over the safety of the Apotex product that they previously received.

CONCLUSION

For the foregoing reasons, Plaintiffs' motion for a preliminary injunction should be denied.

Respectfully submitted,

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